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⑲ Hydrogen peroxide composition.

⑳ An antimicrobial composition containing hydrogen peroxide is disclosed. The composition is non-corrosive to surgical instruments and contains 4%-7% hydrogen peroxide, 0.1% to 0.3% of a chelating agent, 0.1% of a water soluble zinc compound, 0.1% to 0.3% of a sodium lauryl sarcosinate or a fatty acid-based analog, an anionic surfactant selected from the group consisting of sodium n-decyl diphenoxyether disulfonate or sodium lauryl sulfate and a buffer system to maintain the pH of the composition in a pH range of from 4 to 6.

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Hydrogen Peroxide Composition

Field of the Invention

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This invention relates to an improved hydrogen-peroxide-based sterilizing and disinfecting solution which is stabilized to prevent decomposition of hydrogen peroxide and to prevent corrosion damage to medical instruments 10 contacted with the solution.

Background of the Invention

It has long been recognized that hydrogen peroxide can be 15 employed as an antimicrobial agent to sterilize and disinfect environmental surfaces and surgical instruments. However, hydrogen peroxide has not been extensively used as an antimicrobial agent for hospital equipment because of its instability and because it tends to corrode 20 surgical instruments. Aqueous solutions of hydrogen peroxide are inherently corrosive to a variety of metals such as iron, nickel, copper, chromium and their alloys. Corrosion of these metals when in contact with a hydrogen peroxide solution produces ions which catalyze the 25 decomposition of hydrogen peroxide and accelerate the loss of the antimicrobial activity of the solution. The decomposition of hydrogen peroxide is accompanied by the release of the oxygen which, if allowed to accumulate in a closed container, can create a fire or explosion hazard.

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There have been numerous attempts to stabilize hydrogen peroxide to prevent its rapid decomposition.

35 U.S. Patent 3,053,634 discloses a composition containing hydrogen peroxide, a chelating agent, an aluminum compound and a phosphate salt.

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U.S. Patent 2,961,306 discloses a composition containing 50%/80% hydrogen peroxide and 0.001%-1% 1,2-diaminocyclohexane tetraacetic acid.

5 U.S. Patents 3,089,753 and 3,208,825 disclose compositions having pH values of about 3.3 and 2.5, respectively, containing hydrogen peroxide, a chelating agent, a tin compound such as Na_2SnO_3 and a phosphate salt.

10 U.S. Patent 2,680,674 discloses a composition containing hydrogen peroxide and a zinc or cadmium compound such as the sulfate, nitrate or chloride.

15 Kassem et al. disclose the use of ethylenediamine tetraacetic acid to stabilize hydrogen peroxide against the catalytic effects of iron and zinc. See Chemical Abstracts 78:164666H and 78:164667J.

20 We have found that the stabilizer systems mentioned in the above-cited references are insufficient to prevent the corrosion of surgical instruments or the decomposition of hydrogen peroxide when the hydrogen peroxide solution is used as a sterilizing and disinfecting agent.

25 Summary of the Invention

30 The present invention provides a sterilizing and disinfecting solution in which hydrogen peroxide is the active ingredient and in which the solution is stabilized against the decomposition of the hydrogen peroxide and which solution will not excessively corrode surgical instruments. The solution has excellent sterilization and disinfecting properties and can be used to sterilize sophisticated medical instruments such as endoscopes.

35 The present composition contains a number of ingredients

each of which is necessary in the composition to produce the desired result. These ingredients are the following:

1. Hydrogen Peroxide.

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2. A nitrogen-containing chelating agent such as N-(hydroxyethyl)ethylenediamine-triacetic acid (HEEDTA), ethylenediamine-tetraacetic acid (EDTA), or diethylenetriamine-pentaacetic acid (DTPA) or their 10 sodium salts.

3. A water soluble zinc compound such a zinc sulfate, zinc acetate, zinc nitrate or zinc gluconate.

15 4. A sarcosinate surfactant such as sodium cocoyl sarcosinate or sodium lauryl sarcosinate.

5. An anionic surfactant selected from the group consisting of sodium n-decyl diphenylether disulfonate or 20 sodium lauryl sulfate.

25 6. A buffer composition such as sodium acetate, sodium phosphate, sodium borate or mixtures thereof to maintain the pH of the aqueous solution at a level of from pH 4.5 to pH 5.5.

Detailed Description of the Invention

The compositions of this invention are aqueous solutions containing the following ingredients: (all percentages 30 are by weight based on the total weight of the solution)

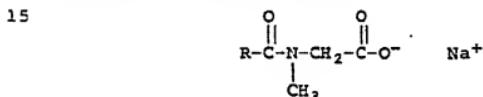
(1) Hydrogen peroxide (H_2O_2), in a concentration between 4% and 7%.

35 (2) A nitrogen-containing chelating agent such as N-(hydroxyethyl)-ethylenediaminetriacetic acid (HEEDTA),

ethylenediaminetetraacetic acid (EDTA), and diethylene-triaminepentaacetic acid (DTPA) or their sodium salts, in a concentration from 0.1% to 0.39%.

5 (3) A soluble compound containing zinc ions such as zinc sulfate, zinc acetate, zinc nitrate or zinc gluconate in a concentration of about 0.1%. The presence of the zinc in the formulation provides improved corrosion inhibition against copper and nickel and maintains the 10 transparency of the solution. The preferred zinc compound is zinc sulfate heptahydrate.

(4) Sodium cocoyl sarcosinate and its fatty acid-based analogs of the structure:



20 where R is a hydrocarbon chain having between 11 and 14 carbon atoms. These are employed at a concentration of 0.1% to 0.3%.

25 (5) An anionic surfactant selected from the group consisting of sodium n-decyl diphenylether disulfonate and sodium lauryl sulfate in a concentration from 0.1% to 0.3%.

30 (6) A buffer operating in the pH range from 4 to 6, such as sodium acetate, sodium phosphate and sodium borate. The buffer concentration range may be 0.5% or below.

35 It has been found that all of the above-mentioned ingredients are necessary in order to obtain a satisfactory solution with the desired stability, non-corrosiveness and antimicrobial properties.

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A composition containing the above-mentioned ingredients provides excellent antimicrobial activity and does not excessively corrode surgical instruments. The composition can be used at room temperatures and at elevated temperatures, e.g., 40°C to 50°C. The antimicrobial activity of the composition is enhanced if the composition is employed at an elevated temperature. At elevated temperatures, the composition will disinfect and sterilize in a shorter time period than at room temperature. However, the composition is an effective disinfecting solution at room temperatures in reasonable time periods.

In addition to the ingredients specified above, the composition of the present invention may also contain option inactive ingredients such as a dye, for example FD&C Yellow #5. The present composition may be packaged as a single component with all the ingredients in one container or may be packaged as a two-component system. As a two-component system, the hydrogen peroxide is mixed with water and placed in one container. The remaining ingredients are placed in a second container with a small amount of water, and the contents of the two containers are thoroughly mixed immediately prior to use. When the two-component system is used, a small amount of a surfactant, which is a condensate of ethylene oxide with propylene glycol and propylene oxide, e.g., PLURONIC P104 (BASF Wyandotte), may be added to the second container to maintain homogeneity of the ingredients.

The sporicidal test employed in the following Examples is the A.O.A.C. Sporicidal Test as specified in Official Methods of Analysis of the Association of Official Analytical Chemists (A.O.A.C.) 13th Edition, 1980 Sections 4.015-4.017. The Use Dilution Test is employed in Sections 4.007-4.011; The Fungicidal Test is employed in

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Sections 4.018-4.022, and the Tuberculocidal Test is employed in Sections 4.048-4.050 of the same publication.

5 In the Examples, all percentages are weight percent unless otherwise indicated.

Example I

10 This Example shows that the compositions of the present invention have excellent antimicrobial properties, and the compositions do not cause corrosion of surgical instruments.

15 Two solutions containing 6% hydrogen peroxide were prepared according to the formulations set forth in Table IA.

Table 1A

20 Compositions of Sterilizing/Disinfecting Solutions

	<u>Ingredients</u>	<u>Formulation I</u> (Weight Percent)	<u>Formulation II</u> (Weight Percent)
25	Hydrogen peroxide	6.0	6.0
	Acetic Acid	<u>ca.</u> 0.1	<u>ca.</u> 0.1
	Zinc sulfate (7H ₂ O)	0.1	0.1
	HEEDTA*	0.3	0.3
	Sodium cocoyl sarcosinate	0.3	0.3
30	Sodium lauryl sulfate	0.15	---
	Sodium n-decyl diphenylether disulfonate	---	0.15
	Water	remainder	remainder
	Solution pH	5.0	5.0

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*N-(hydroxyethyl)ethylenediamine triacetic acid

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The formulations were tested against various organisms at a temperature of 40°C, and the results are shown in Table 1B.

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Table 1B

10	<u>Organisms</u>	<u>Carriers</u>	Exposure Time (minutes)	Failure Rates in AOAC Sporicidal or Use Dilution Tests	
				Form. I	Form. II
				<u>Sporicidal Test</u>	
15	<u>B. subtilis</u> spores	porcelain	30	0/60	0/60
			45	0/60	0/60
			60	0/60	0/60
20	<u>C. sporogenes</u> spores	silk suture	30	1/60	0/60
			45	1/60	0/60
			60	0/60	0/60
25		porcelain	30	2/60	2/60
			45	1/60	0/60
			60	0/60	0/60
<u>Use Dilution Test</u>					
30	<u>S. aureus</u>	stainless steel	10	1/60	0/60
35	<u>P. aeruginosa</u>	stainless steel	10	0/60	0/60
35	<u>S. cholerae</u>	stainless steel	10	0/60	0/60

In an AOAC Sporicidal Test, one failure in 60 is not acceptable.

5 The Environmental Protection Agency considers a failure rate of 1/60 in a Use Dilution Test as above the minimum requirement of a passing test.

10 The corrosion properties of the Formulation I and II solutions were tested by immersing a carbon steel scalpel blade, a brass fitting, a "nickel silver" skin closure clip and a pair of chrome-plated scissors in the respective solution in a glass container at a temperature of 40°C. The results are shown in Table 1C. ("Nickel silver" is an alloy of copper, nickel and zinc.)

15

Table 1C

Corrosion/Stability Studies on Hydrogen Peroxide Sterilizing/Disinfecting Solutions at 40°C.

20

Observations	Formulation I	Formulation II	Comm. Available Hydrogen Peroxide Solution-After
	After 6 days	After 6 days	3 Hours
hydrogen peroxide	6.30%	6.02%	—
pH	5.4	5.3	<u>ca.</u> 1.8
precipitate	none	none	heavy ppt.
carbon steel	untarnished	untarnished	untarnished
brass	untarnished	untarnished	tarnished
nickel silver	untarnished	untarnished	tarnished
chrome	untarnished	untarnished	—

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The presence of a precipitate in the solution indicates that the metal has been removed from the samples and precipitated from the solution.

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Example 2

A formulation of the present invention containing:

6% hydrogen peroxide

0.2% HEEDTA

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0.15% sodium n-decyl diphenylether disulfonate (DOWFAX 3B2, Dow Chemical Co.)

0.3% sodium cocoyl sarcosinate

0.1% $ZnSO_4 \cdot 7H_2O$

15

water to 100%

The formulation also contained sufficient acetic acid to give a resultant pH of 5.0 and 0.1% of a nonionic surfactant which consists of condensates of ethylene oxide with 20 propylene glycol and propylene oxide (PLURONIC F104).

The formulation was tested against various organisms at 20°C. In some tests the formulation was diluted with water in a ratio of 1 part formulation to 2 parts water 25 to determine the effect of the dilution on the activity. The results are presented in Table 2. The results show that at a peroxide concentration of 3% (1:2 dilution), the formulation is not effective against certain organisms, i.e., *S. aureus* and *M. tuberculosis*.

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Table 2

	<u>Microorganisms</u>	<u>Exposure Time (Min.)</u>	<u>Dilution</u>	<u>Failure Rate</u>
5	<u>S. aureus</u> ^a	10	undiluted	5/30
		20	undiluted	0/60
		20	1:2	44/60
10	<u>P. aeruginosa</u> ^a	20	undiluted	1/60
		20	1:2	1/60
15	<u>S. choleraesuis</u> ^a	20	undiluted	0/60
		20	1:2	0/60
20	<u>T. mentagrophytes</u> ^b	5	undiluted	passed
		10	undiluted	passed
		15	undiluted	passed
		5	1:2	passed
		10	1:2	passed
		15	1:2	passed
25	<u>M. tuberculosis</u> ^c	20	undiluted	0/80
		20	1:2	30/80

The Environmental Protection Agency considered a failure rate of 1/60 as a "pass" for A.O.A.C. Use Dilution Test.

30 ^aA.O.A.C. Use Dilution Test

^bA.O.A.C. Fungicidal Test

^cA.O.A.C. Tuberculocidal Test

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Example 3

This Example shows that the amount of hydrogen peroxide in the formulation may be reduced to 4% without any reduction in sporidical activity. Formulations were prepared at 5% and 4% hydrogen peroxide concentrations. In addition to the hydrogen peroxide, the formulations contained:

15 The solutions were adjusted to pH 5 with acetic acid or sodium hydroxide.

The solutions were tested against various spores at 40°C with exposure times of 45 minutes. The results of the tests are given in Table 3.

Table 3

25	<u>Spores</u>	<u>% H₂O₂</u>	<u>Carriers</u>	<u>Failure Rates</u>
30	<u>B. subtilis</u>	5	Suture	0/30
			Porcelain	0/30
35	<u>C. sporogenes</u>	4	Suture	0/30
			Porcelain	0/30
35		5	Suture	0/30
			Porcelain	0/30
35		4	Suture	0/30
			Porcelain	0/30

Example 4

In order to show the necessity of various ingredients in the present solution, a series of 29 formulations were prepared with some ingredients omitted or the concentrations changed. All of the formulations contained 6% hydrogen peroxide. The composition of the formulations is shown in Table 4A. The corrosiveness of the formulations was then determined by immersing metal specimens in the solutions at 40°C for six days. The metal specimens included a carbon steel scalpel blade, a "nickel silver" skin closure clip and a copper fitting. A solution is not acceptable if the solution transparency is poor; if there is a heavy precipitate; if the dissolved metal is greater than 100 ppm; or, if the metal specimens are indicated to be poor. The solutions in which the final pH was above 6 is a result of a high initial pH or a high level corrosion of the metal and the loss of hydrogen peroxide. The results of the testing is shown in Table 4B.

An examination of the results set forth in Tables 4A and 4B indicates that hydrogen peroxide solutions must contain the surfactants and chelating agent specified herein and be maintained at the proper pH in order to obtain the desired non-corrosive properties.

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Table 4A

No.	ZnSO ₄ ·7H ₂ O (%)	Surfactants (% active)			Chelating Agent		Initial pH	Final pH
		A	B	C	Type	%		
1	.1	.3	.15	.1	HEEDTA	.3	5.0	5.0
2	.1	.3	—	.1	HEEDTA	.3	5.0	5.2
3	.1	—	.15	.1	HEEDTA	.3	5.0	8.0
4	.1	—	—	.1	HEEDTA	.3	5.0	8.7
5	—	.3	.15	.1	HEEDTA	.3	5.0	4.6
6	—	.3	.15	.1	—	—	5.0	4.1
7	.1	.3	.15	.1	HEEDTA	.1	5.0	5.1
8	.1	.3	.15	.1	HEEDTA	.2	5.0	4.9
9	.1	.3	.15	.1	HEEDTA	.4	5.0	4.9
10	.1	.1	.15	.1	HEEDTA	.3	5.0	4.9
11	.1	.4	.15	.1	HEEDTA	.3	5.0	5.0
12	.1	.3	.15	.1	HEEDTA	.3	3.3	5.0
13	.1	.3	.15	.1	HEEDTA	.3	4.0	4.2
14	.1	.3	.15	.1	HEEDTA	.3	6.0	8.2
15	.1	.3	.15	.1	HEEDTA	.3	7.0	8.1
16	.1	.3	.15	—	HEEDTA	.3	5.0	5.0
17	.1	.3	.15	.1	EDTA	.1	5.0	5.0
18	.1	.3	.15	.1	EDTA	.2	5.0	5.2
19	.1	.3	.15	.1	EDTA	.3	5.0	5.0
20	.1	.3	.15	.1	EDTA	.4	5.0	4.7
21	.1	.3	.15	.1	DTPA	.1	5.0	4.4
22	.1	.3	.15	.1	DTPA	.2	5.0	4.9
23	.1	.3	.15	.1	DTPA	.3	5.0	5.2
24	.1	.3	.15	.1	DPA	.4	5.0	7.6
25	.1	.3	.15	.1	DPA	.5	5.0	7.3
26	.1	.3	.15	.1	DTPA	.3	4.0	4.9
27	.1	.3	.15	.1	DTPA	.3	4.5	4.8
28	.1	.3	.15	.1	DTPA	.3	5.5	4.8
29	.1	.3	.15	.1	DTPA	.3	6.0	4.8

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A - Sodium cocyl sarcosinate

B - Sodium n-decyl diphenylether disulfonate

C - Nonionic surfactant - condensate of ethylene oxide
with propylene glycol and propylene oxide.

Table 4B

No.	H ₂ O ₂ %	Loss of Solution			Dissolved Metals(ppm)			Metal Specimens
		Transparency	Color	Precipitate	Fe	Cu		
1	9	fair	sl.blue	none	.45	65.1	good	
2	7	poor	sl.blue	none	.40	65.1	good	
3	100	fair	sl.green	heavy	.10	103	poor	
4	100	fair	sl.yellow	heavy	.15	48.3	poor	
5	18	poor	colorless	none	.50	77.7	good	
6	26	poor	colorless	none	.30	54.6	good	
7	8	good	colorless	none	.30	23.1	good	
8	0	fair	sl.blue	none	.40	54.6	good	
9	5	fair	sl.blue	none	.50	103	good	
10	4	excellent	sl.blue	none	.40	50.4	good	
11	12	poor	sl.blue	none	.50	77.7	good	
12	8	good	blue	none	.20	2,778	poor	
13	6	poor	sl.blue	none	.60	176	good	
14	9	good	sl.green	heavy	.15	109	poor	
15	4	fair	sl.green	heavy	.10	134	poor	
16	7	fair	sl.blue	none	.4	65.1	good	
17	0	good	colorless	none	.25	19	good	
18	0	good	sl.blue	none	.20	81	good	
19	2	fair	sl.blue	none	.20	109	fair	
20	4	fair	sl.blue	none	.25	55	good	
21	0	good	sl.blue	none	.25	63	fair	
22	0	good	colorless	none	.25	40	good	
23	0	excellent	colorless	none	.20	25	good	
24	100	poor	blue	heavy	.10	380	poor	
25	100	poor	blue	heavy	.15	410	poor	
26	0	good	colorless	none	.25	36	good	
27	3	good	colorless	none	.25	44	good	
28	0	good	colorless	none	.25	40	good	
29	0	good	colorless	none	.25	42	good	

Claims

1. An aqueous disinfecting solution having a buffered pH of from 4 to 6.0 comprising from 4% to 6% by weight 5 hydrogen peroxide, from 0.1% to 0.3% by weight of an anionic surfactant selected from the group consisting of sodium lauryl sulfate and sodium n-decyl diphenylether disulfonate; from 0.1% to 0.3% by weight of a sarcosinate surfactant selected from the group consisting of sodium 10 cocoyl sarcosinate and sodium lauryl sarcosinate; 0.1% by weight of a soluble zinc compound selected from the group consisting of zinc sulfate, zinc acetate, zinc nitrate and zinc gluconate and from 0.1% to 0.3% by weight of a nitrogen containing chelating agent selected from the 15 group consisting of N-(hydroxy-ethyl) ethylenediamine triacetic acid, ethylenediamine tetracetic acid and diethylenetriamine pentaacetic acid.
2. An aqueous disinfecting solution of Claim 1 in which 20 the anionic surfactant is sodium n-decyl diphenyl ether disulfonate; the sarcosinate surfactant is sodium cocoyl sarcosinate; and, the soluble zinc compound is zinc sulfate, and the chelating agent is N-(hydroxyl-ethyl) ethylenediamine triacetic acid.
3. A process of disinfecting metallic surgical instruments comprising contacting said instruments with a 25 solution according to claim 1 or claim 2.
4. A process for preparing an aqueous disinfecting solution according to claim 1 comprising mixing from 30 4% to 6% by weight hydrogen peroxide, from 0.1% to 0.3% by weight of an anionic surfactant selected from the group consisting of sodium lauryl sulfate and sodium n-decyl diphenylether disulfonate; from 0.1% to 0.3% by weight of a sarcosinate surfactant selected from the 35 group consisting of sodium cocoyl sarcosinate and sodium lauryl sarcosinate ; 0.1% by weight of a soluble zinc compound selected from the group consisting of zinc sulfate, zinc

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acetate, zinc, nitrate and zinc gluconate and from 0.1% to 0.3% by weight of a nitrogen containing chelating agent selected from the group consisting of N-(hydroxy-ethyl) ethylenediamine triacetic acid, ethylenediamine tetracetic acid and diethylenetriamine penacetic acid with water and buffering the solution to a pH from 4 to 6.0.



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⑩ Hydrogen peroxide composition.
⑦ An antimicrobial composition containing hydrogen peroxide is disclosed. The composition is non-corrosive to surgical instruments and contains 4%–7% hydrogen peroxide, 0.1% to 0.3% of a chelating agent, 0.1% of a water soluble zinc compound, 0.1% to 0.3% of a sodium cocoyl sarcosinate or its fatty acid-based analogs, an anionic surfactant selected from the group consisting of sodium n-decyl diphenylether disulfonate or sodium lauryl sulfate and a buffer system to maintain the pH of the composition in a pH range of from 4 to 6.

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EUROPEAN SEARCH REPORT

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Application number

EP 83 30 6894

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.)
A	US-A-4 155 738 (M.P. BOGHOSIAN) * Claims *	1	C 11 D 3/48 C 01 B 15/037 A 01 N 59/00
A	FR-A-2 085 899 (BP CHEMICALS) * Claims *	1	

			TECHNICAL FIELDS SEARCHED (Int. Cl.)
			C 11 D A 01 N C 01 B
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
THE HAGUE	03-06-1986	GOLLER P.	
CATEGORY OF CITED DOCUMENTS			
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p>			
<p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			